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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/781,069 | 02/18/2004 | Armin Meinzer | 100-8388C | 1856 |

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
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| EXAMINER | |
|---|---|
| CHANNAVAJJALA, LAKSHMI SARADA | |

| ART UNIT | PAPER NUMBER |
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| 1611 | |

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| 02/26/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/781,069 | MEINZER ET AL. | |
| | Examiner | Art Unit | |
| | Lakshmi S. Channavajjala | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-2-07 has been entered.

2. Claim 25 has been canceled. Claims 12-24 and 26 are pending.

Instant claims are now amended to recite "wherein less than 5% of oils apart from those present in the surfactant, are present in the composition", that is supported on page 2, lines 9-12.

The following rejections of record have been maintained:

***Double Patenting***

Claims 12-24 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,432,445 ('445) in view of US 5,962,019 ('019). '445 claim a capsule comprising cyclosporin, a polyoxyethylene sorbitan fatty acid ester, a reaction product of a natural or hydrogenated castor oil and ethylene glycol and ethanol. Component C of the '445 capsule reads on the instant surfactant. '445 capsules do not contain the polyethylene glycol of the instant claims.

'019 teach hard gelating capsules comprising cyclosporin formulations (abstract, col. 3 L 10-25). '019 teaches that the compositions contain an orally acceptable vehicle comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols (col. 4, L 28-41). Among the diols, '019 teach the claimed polyethylene glycols (col. 5, L 1-25 and examples in col. 8-10). '019 further teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Thus, both '445 and '019 are directed to cyclosporin containing capsule formulations. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to include polyethylene glycol, of '019 in the cyclosporin composition of '445 as a co-solvent for the lower alkanol solvent of '445 because '019 teach that the polyethylene glycol co-solvents adsorb water molecules, which may be present in the formulations thereby reducing the possibility for precipitation of the cyclosporin from the formulations, and also impart desirable properties such as viscosity, stability etc. Accoridngly, a skilled artisan would have expected to achieve greater stability of the composition of '445 by incorporating the PEG of '019.

Claims 12-24 and 26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,767,555 ('445) in view of US 5,962,019 ('019).

'555 claim a capsule comprising cyclosporin, a polyoxyethylene sorbitan fatty acid ester, a reaction product of a natural or hydrogenated castor oil and ethylene glycol

and ethanol. Component C of the '555 capsule reads on instant surfactants. '555 capsules do not contain the polyethylene glycol of the instant claims.

'019 teach hard gelating capsules comprising cyclosporin formulations (abstract, col. 3 L 10-25). '019 teaches that the compositions contain an orally acceptable vehicle comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols (col. 4, L 28-41). Among the diols, '019 teach the claimed polyethylene glycols (col. 5, L 1-25 and examples in col. 8-10). '019 further teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Thus, both '555 and '019 are directed to cyclosporin containing capsule formulations. It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to include polyethylene glycol, of '019 in the cyclosporin composition of '555 as a co-solvent for the lower alkanol solvent of '555 because '019 teach that the polyethylene glycol co-solvents adsorb water molecules, which may be present in the formulations thereby reducing the possibility for precipitation of the cyclosporin from the formulations, and also impart desirable properties such as viscosity, stability etc. Accoridngly, a skilled artisan would have expected to achieve greater stability of the composition of '555 by incorporating the PEG of '019.

## *Claim Rejections - 35 USC § 103*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 12-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,342,625 to Hauer et al (Hauer) in view of US 5,962,019 ('019) to Cho.

Hauer teaches cyclosporin comprising pharmaceutical compositions in the form of microemulsion pre-concentrates and that are filled in hard gelatin capsules (abstract, examples, col. 29, lines 11-14). Examples in col. 26-29 are directed cyclosporin formulation, which include surfactants Cremophor RH 40, which is described as a reaction product of hydrogenated or natural vegetable oil and ethylene glycol, with an HLB value of 14-16. Thus, the surfactant of Hauer meets the claimed surfactant component. Hauer also teaches composition comprising propylene glycol and ethanol that read on the claimed lower alkanols (col. 18, last paragraph to col. 19, 1st paragraph). The pre-concentrate compositions of Hauer are free of water and form spontaneous emulsions (col. 5, lines 57 through col. 6, lines 35) and hence meet the claims 22, 23 and 26. Hauer teaches various amounts of cyclosporin in the examples that is within the claimed ranges (claim 16). Not all of the compositions of Hauer contain additional oils and therefore read on the less than 5% of oils apart from those present in the surfactant.

Hauer fails to teach polyethylene glycol in combination with the lower alkanols. Cho teaches hard gelating capsules comprising cyclosporin formulations (abstract, col. 3 L 10-25). Cho teaches that the compositions contain an orally acceptable vehicle comprising at least one alkanol solvent constituting an alkanol having 2 to 3 carbon atoms and a co-solvent selected from fatty acids and diols (col. 4, L 28-41). Among the diols, Cho teaches the claimed polyethylene glycols (col. 5, L 1-25 and examples in col.

8-10). 'Cho teach incorporating at least one surfactant, such as polyoxyalkylene surfactant having an HLB value of 5 to 20 or preferably 8 to 16. Thus, both Hauer and Cho teach cyclosporin compositions comprising a surfactant and hydrophilic solvents, constituting analogous art. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to include polyethylene glycol, of Cho in the cyclosporin composition of Hauer as a co-solvent for the lower alkanol solvent of because Cho teaches that the polyethylene glycol co-solvents adsorb water molecules, which may be present in the formulations thereby reducing the possibility for precipitation of the cyclosporin from the formulations, and also impart desirable properties such as viscosity, stability etc. Accoridngly, a skilled artisan would have expected to achieve greater stability of the composition of Hauer containing cyclosporin by incorporating the PEG of '019. Further, optimizing the amount of solvents and co-solvents in the composition of Hauer with an expectation to achieve the desired solubility and optimum stability would have been within the scope of a skilled artisan. While Hauer does describe oils, the examples of Hauer do not necessarily contain oils while instant claims recite that less than 5% of oils apart from those present in the surfactant, applicants have not shown any unexpected advantage with the claimed limit of less of than 5%.

***Response to Argument***

Applicant's arguments filed 11-02-07 have been fully considered but they are not persuasive.

Applicants arguments regarding the prior art have been addressed in the previously and are incorporated herewith.

Applicants traverse the rejection and submit that claims 12-26 of the present application do not define an invention that is merely an obvious variation of the invention claimed in the '445 patent. It is argued that none of the claims of the '445 patent suggest a pharmaceutical composition comprising polyethylene glycol and that examiner has not, however, shown that one skilled in the art would find it obvious to limit the compositions to be substantially free of any additional oil, i.e., wherein less than 5% of oils apart from those present in the surfactant, are present in the composition.

It is argued that the '019 patent would suggest to one skilled in the art that additional oils may be used (column 4, lines 42-65), where specific fatty acids are enumerated. However, in the summary section, Cho teaches fatty acids and polyalkylene glycols, preferably polyalkylene glycols. Thus, it is not necessary that both are present and that the latter is preferable (col. 2, L 48-58).

Applicants argue that the while some examples of Hauer include very high amounts of oils (Miglyol etc), other require (examples 4-7) Transcutol or Glycofurol that are not required by the instant application and do not contain polyethylene glycol. However, the arguments are not persuasive because instant claims allow for the presence of additional components such as Transcutol or Glycofurol and further the teachings of Cho have been cited and the motivation for including polyethylene glycol, which is absent in Hauer. The argument that Cho does not teach the instant

surfactant is not persuasive because Cho has not been cited for the surfactant and only for polyethylene glycol. Thus, the resulting composition of Hauer would be free of oils.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner,
Art Unit 1611